

**REMARKS**

**Amendments to the Claims**

Reconsideration of this application is respectfully requested. Upon entry of the foregoing amendment, claims 3-6 and 8-12 remain pending in the application. Claims 8 and 11 are currently amended.

Applicants respectfully request entry of the above amendment and submit that the above amendment does not constitute new matter. Support for amended claims 8 and 11 can be found throughout the specification and in the claims as originally filed. Support for the amendments to claim 8 and 11 can be found, for example, at pages 7-8, page 10, ll. 12-16 and page 11, ll. 18-19 of the specification.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

**Information Disclosure Statement**

Applicants appreciate and thank the Examiner for considering Applicants' First and Second Supplemental Information Disclosure Statements.

Applicants respectfully request the Examiner to consider Applicants' previously-filed Information Disclosure Statement and accompanying PTO/SB/08A submitted on May 10, 2002. A copy of the PTO/SB/08A submitted on May 10, 2002 is attached herewith for the Examiner's convenience as **Exhibit A**. A copy of the date-stamped postcard indicating receipt of Applicants' Information Disclosure Statement and PTO/SB/08A submitted on May 10, 2002 is attached herewith as **Exhibit B**.

**Certified Priority Document**

The Office Action requires the submission of a copy of the certified priority document. (See Office Action at page 2). Applicants respectfully intend to provide a copy of the certified priority document before a patent is granted. (See 37 C.F.R. § 1.55).

**Rejections under 35 U.S.C. § 103(a)**

Claims 3-6 and 8-12 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 5,670,340, issued to Yabuta et al. (“Yabuta”). Applicants respectfully traverse this rejection.

Applicants assert that in order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. (See M.P.E.P. §§ 2142-2143 (8<sup>th</sup> ed., Rev. No. 2)).

The Office Action states that “[i]n Examples 3 and 4 Yabuta et al. teach production of human calcitonin from fusion protein in *E. coli*” and “Examples 5-8 teach production of CNP-22 from fusion protein in *E. coli*.” (See Office Action at page 3). The Office Action further states that Yabuta does not teach the production of ANP from a fusion protein in *E. coli*, but that Yabuta states, “the method can be applied for the production of a fusion protein of physiologically active peptides, for example natriuretic peptides, such as ANP.” (See *id.*). Accordingly, the Examiner concludes that “[i]t would have been obvious to a person of skill in the art to substitute ANP for human calcitonin or CNP as per teachings of Yabuta et al. because the same result should be expected when using ANP in place of CNP or calcitonin.”

Claim 9 is directed to a method of reducing formation of a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue. Claim 9 recites three steps including: (i) culturing transformed host cells that produce a recombinant atrial natriuretic peptide comprising a serine residue and a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue; (ii) adding at least one of histidine, methionine or glycine to reduce said byproduct formation; and (iii) reducing the formation of said byproduct polypeptide. Claim 10 is directed to a method of producing a polypeptide comprising a serine residue and also recites the steps of (i) culturing transformed host cells...; (ii) adding at least one of histidine, methionine or glycine...; and (iii) reducing the formation of said byproduct polypeptide.

Accordingly, in order establish a *prima facie* case of obviousness, Yabuta must teach or suggest each of the three steps in the claimed methods.

Applicants assert that Yabuta fails to teach or suggest each of the three steps recited in the claimed methods. For example, Yabuta does not teach or suggest the step of adding at least one of histidine, methionine or glycine to reduce byproduct formation or the step of reducing the formation of said byproduct polypeptide. In addition, the Office Action fails to point out where Yabuta teaches or suggests all of the elements contained in the culture media of claims 11 or 12. Accordingly, because Yabuta does not teach or suggest each and every claim limitation, Yabuta does not render claims 3-6 and 8-12 obvious.

Applicants note that on page 4, the Office Action states:

Claim 9 is rejected because the preamble states “a method for reducing formation of a by product comprising an o-acetylserine residue in place of a serine residue, comprising...” however the invention only requires culturing transformed host cells in a medium comprising at least one histidine, methionine or glycine in an amount effective to reduce the formation of a byproduct polypeptide. The recitation of o-acetylserine is limited to the preamble of the claims or as the inherent end-point of the claimed method. *In re Hirao*, 535 F.2d 67, 190 USPQ (CCPA 1976), the court states that a preamble is generally not accorded (sic) any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness, but instead, the process steps or structural limitation are able to stand alone.

Applicants submit that contrary to the Office Action’s assertion that “the invention only requires culturing transformed host cells in a medium comprising at least one histidine, methionine or glycine...,” claim 9 recites three method steps as outlined above. Applicants also submit that contrary to the Office Action’s assertion that “[t]he recitation of o-acetylserine is limited to the preamble of the claims or as the inherent end-point of the claimed method,” step (i) of claim 9, recites, “culturing, in a medium, transformed host cells that produce...*a byproduct polypeptide comprising an O-acetylserine residue* in place of a serine residue” and step (iii) of claim 9 recites, “reducing the formation of *said byproduct polypeptide*.” (emphasis added). Accordingly, Applicants respectfully submit that the Office Action improperly limits claim 9.

Applicants also note that on page 4, the Office Action states:

In Claims 10-12, the Applicant claims o-acetylserine as a byproduct formed in the method of production of an atrial natriuretic peptide comprising a serine residue. MPEP section 2105 states that language that suggests or makes optional, but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation. For example, a language that may raise a question as to the limiting effect of the language in a claim are statements of intended use or field of use. In claims 10-12, the byproduct o-acetylserine has no effect on the steps performed in the method, therefore o-acetylserine does not limit the claims.

Applicants respectfully submit that MPEP § 2105, which is titled, “Patentable Subject Matter — Living Subject Matter,” does not state or provide any discussion regarding “language that suggests or makes optional, but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation.” Furthermore, it is not clear where the Office Action supports its assertion that “language that may raise a question as to the limiting effect of the language in a claim are statements of intended use or field of use.” It is also unclear as to what is meant by the Office Action’s statement that “the byproduct o-acetylserine has no effect on the steps performed in the method.” Applicants respectfully point out that claim 10, for example, recites “byproduct” in steps (i), (ii) and (iii). Accordingly, Applicants submit that the Office Action’s statements on page 4 of the Office Action do not render claims 10-12 obvious.

For the foregoing reasons, Applicants respectfully request the Examiner to withdraw all of the 103(a) rejections over Yabuta.

## CONCLUSION

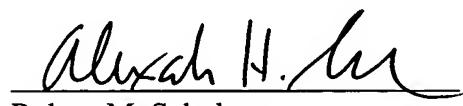
Applicants respectfully request consideration of the above remarks. In view of the above remarks, early notification of a favorable consideration is respectfully requested.

A check is enclosed in the amount of \$450.00, which covers the two-month extension of time fee. The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-0206.

Respectfully submitted,

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